REMARKS

Reconsideration of the present application in view of the above amendments and the following remarks is respectfully requested.

Claims 21-32, 34-36, 38-43, 45-59, 61-63 and 65-71 are pending. Claims 21, 23, 32, 36, 40, 45, 49, 53, 59, 63 and 67 have been amended to enter minor changes. Such amendments have been made without acquiescing to the rejections in the Office Action. Support for the amendments to claims 21 and 45 may be found, for example, in the examples of the present application. No new matter has been added via the claim amendments.

Rejections Under 35 U.S.C. 103(a)

Claims 21-27, 30-32, 34-36, 38-40, 42, 43, 45-54, 57-59, 61-63, 65-67 and 69-71 stand rejected under 35 U.S.C. 103(a) as unpatentable over Deggerdal *et al.* (WO 96/18731, "Deggerdal") in view of Nargessi (U.S. Patent No. 6,855,499, "Nargessi").

Applicants respectfully traverse this ground of rejection. Applicants submit that the cited references, either alone or in combination, fail to teach or suggest the methods claimed in the present application. More specifically, there is no sufficient motivation for one of ordinary skill in the art to combine Deggerdal with Nargessi. Contrary to the assertion in the Office Action, Deggerdal itself in fact teaches away from being combined with Nargessi. Deggerdal teaches that increasing viscosity of a sample is detrimental to RNA purification. For example, Deggerdal states that DNA contamination in a sample for RNA purification should be avoided because DNA increases viscosity, which makes sample handling difficult and in turn leads to RNA with poor yield and quality (*see*, the paragraph bridging pages 1 and 2). Deggerdal further provides that "[a] particularly advantageous embodiment of the invention is to use the isolation method of the invention to remove DNA from a sample prior to isolation of RNA, such that the viscosity of the lysed sample is reduced and a specific isolation of RNA molecules is favored which again reduces and avoids the possibility for DNA contamination of the RNA" (emphasis added) (*see*, first full paragraph on page 14). Nargessi is directed to a method for isolating nucleic acid using magnetic or paramagnetic particles encapsulated in a polymer such as

cellulose or its derivatives (*see*, Abstract and column 1, lines 46-52). Such particles adsorb nucleic acids in the presence of a salt and polyalkylene glycol (preferably polyethylene glycol with an average molecular weight of 8,000 (PEG 8000 MW)) at appropriate concentrations formulated as a binding buffer (column 4, lines 4 to 36). Because the binding of nucleic acid to the magnetic or paramagnetic particles requires the presence of both the salt and polyalkylene glycol in Nargessi, to modify Deggerdal in view of Nargessi, one has to add polyalkylene glycol to the lysing/binding buffer of Deggerdal. Because, as discussed above, Deggerdal teaches away from increasing the viscosity of the lysing/binding buffer and because including a polyalkylene glycol, such as 10% PEG 8000 MW used throughout the examples of Deggerdal, in the lysing/binding buffer would significantly increase the viscosity of the lysing/binding buffer, one of ordinary skill in the art would not have combined Deggerdal with Nargessi.

Claims 41 and 68 stand rejected under 35 U.S.C. 103(a) as unpatentable over Deggerdal in view of Nargessi and further in view of the Calbiochem 2000-2001 reagent catalog.

Applicants respectfully traverse this ground of rejection. As discussed above, Deggerdal and Nargessi, either alone or in combination, fail to teach or suggest the method according to claim 21 or claim 45 of the present application to which claims 41 and 68 ultimately refer. Calbiochem 2000-2001 only relates to detergents and thus fails to remedy the deficiencies of Deggerdal and Nargessi.

Claims 28, 29, 55 and 56 stand rejected under 35 U.S.C. 103(a) as unpatentable over Deggerdal in view of Nargessi and further in view of Heath *et al.* (WO 99/39009, "Heath").

Applicants respectfully traverse this ground of rejection. As discussed above, Deggerdal and Nargessi, either alone or in combination, fail to teach or suggest the method according to claim 21 or claim 45 of the present application to which the rejected claims directly or indirectly refer. Heath relates to DNA isolation and fails to remedy the deficiencies of Deggerdal and Nargessi.

Claims 21-26, 30-32, 34-36, 38-40, 42, 43, 45-53, 57-59, 61-63, 65-67 and 69-71 stand rejected under 35 U.S.C. 103(a) as unpatentable over Deggerdal in view of Lader (U.S. Patent No. 6,204,375, "Lader").

Applicants respectfully traverse this ground of rejection. Applicants submit that Deggerdal and Lader, either alone or in combination, do not teach or suggest the methods claimed in the present application. More specifically, the combination of Deggerdal and Lader would not have arrived at the methods claimed in the present application. Lader is directed to a method for preserving and protecting RNA of tissue samples from degradation prior to RNA isolation using an RNA preservation medium (*see*, Abstract and column 3, lines 35-39). The RNA preservation medium may comprise a salt at a high concentration (*see*, column 3, line 47 to column 4, line 14). To isolate RNA from samples treated with an RNA preservation medium, tissue samples are transferred into tissue extraction buffer (*see*, column 10, lines 16-18). For example, in Example 8, although tissue samples were initially stored in RNAlater™ solution that comprises ammonium sulfate at a high concentration (*see*, Example 2), they were subsequently placed in a guanidinium isothiocyanate lysis solution and homogenized before RNA isolation. In other words, RNA isolation was performed in the guanidinium isothiocyanate lysis solution, not in RNAlater™ solution. Lader also provides that cells in suspension must be pelleted by centrifugation, and then resuspended in an RNA extraction buffer (see, column 10, lines 18-20). Thus, although Lader teaches the presence of a salt at a high concentration in an RNA preservation medium, it fails to teach or suggest the presence of a salt at a high concentration (*e.g.*, greater than about 4 M) in an RNA Lysing Solution. Accordingly, one of ordinary skill in the art would not have been motivated by Lader to modify Deggerdal by including a salt at a high concentration in an RNA lysing/binding solution.

Claims 41 and 68 stand rejected under 35 U.S.C. 103(a) as unpatentable over Deggerdal in view of Lader and further in view of the Calbiochem 2000-2001 reagent catalog.

Applicants respectfully traverse this ground of rejection. As discussed above, Deggerdal and Lader, either alone or in combination, fail to teach or suggest the method according to claim 21 or claim 45 of the present application to which claims 41 and 68 ultimately

refer. Calbiochem 2000-2001 only relates to detergents and thus fails to remedy the deficiencies of Deggerdal and Lader.

Claims 27-29 and 54-56 stand rejected under 35 U.S.C. 103(a) as unpatentable over Deggerdal in view of Lader and further in view of Heath.

Applicants respectfully traverse this ground of rejection. As discussed above, Deggerdal and Lader, either alone or in combination, fail to teach or suggest the method according to claim 21 or claim 45 of the present application to which the rejected claims directly or indirectly refer. Heath relates to DNA isolation and fails to remedy the deficiencies of Deggerdal and Lader.

In view of the above remarks, Applicants submit that the above ground of rejection under 35 U.S.C. 103(a) has been overcome. Withdrawal of these rejections is respectfully requested.

Double Patenting Rejection

Claims 21-32, 34-36, 38-43, 45-59, 61-63 and 65-71 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as unpatentable over claims 1-85 of co-pending Application No. 11/589,364.

To facilitate allowance and without acquiescing to the rejection in the Office Action, Applicants submit herewith a terminal disclaimer in compliance with 37 CFR 1.321(c). Accordingly, this ground of rejection has been overcome. Withdrawal of this rejection is respectfully requested.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants believe that all of the claims remaining in the application are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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